WE CLAIM:

1. A composition comprising:

a) interferon conjugated to a polyalkylene oxide polymer having a molecular weight of at least about 12 kDa; and optionally

b) a surfactant;

c) an excipient, and

d) a buffer

wherein the pH range of the solution is from about 3 to about 11.

2. The composition of claim 1 wherein the interferon is interferon-*beta* 1b.

3. The composition of claim 1 wherein the surfactant is selected from the group consisting of polyoxyethylene sorbitol esters and polyethylene glycol.

4. The composition of claim 1 wherein the pH range is from about 2.5 to about 8.5.

5. The composition of claim 1 wherein the pH range is from about 3.0 to about 5.0.

6. The composition of claim 1 wherein the pH range is from about 3.0 to about 4.0.

7. The composition of claim 1 wherein the buffer is selected from the group consisting of Glycine-HCl, acetic acid, sodium acetate, sodium aspartate, sodium citrate, sodium phosphate and sodium succinate.

8. The composition of claim 1 wherein the buffer is selected from sodium acetate, sodium citrate and glycine HCl.

9. The composition of claim 1 wherein the buffer has an ionic strength of about 10mM.

10. The composition of claim 1 wherein the buffer is present in a concentration of from about 3 mM to about 10 mM.

11. The composition of claim 1 wherein the excipient is non-ionic and is selected from the group consisting of, monosaccharides, disaccharides, and alditols.

12. The composition of claim 7 wherein the excipient is selected from the group consisting of glucose, ribose, galactose, D-mannose, sorbose, fructose, xylulose, sucrose, maltose, lactose, trehalose, raffinose, maltodextrins, dextrans, glycerol, sorbitol, mannitol, and xylitol.

13. The composition of claim 8 wherein the excipient is selected from the group consisting of sucrose, trehalose, mannitol and glycerol or a combination thereof.

14. The composition of claim 9 wherein the excipient is selected from the group consisting of mannitol and sucrose or a combination thereof.

15. The composition of claim 1 wherein the surfactant is non-ionic and is selected from the group consisting of polysorbate 80, polysorbate 20, and polyethylene glycol.

16. The composition of claim 1 wherein the polyalkylene oxide polymer is linear or branched.

17. The composition of claim 1 wherein the linear polyalkylene oxide polymer is of the formula:

$$A\text{-}O\text{-}(CH_2CH_2O)_x\text{-}$$
$$A\text{-}O\text{-}(CH_2CH_2O)_x\text{-}CH_2C(O)\text{-}O\text{-},$$
$$A\text{-}O\text{-}(CH_2CH_2O)_x\text{-}CH_2CH_2NR_7\text{-},$$
$$A\text{-}O\text{-}(CH_2CH_2O)_x\text{-}CH_2CH_2SH,$$

$$\text{-}O\text{-}C(O)CH_2\text{-}O\text{-}(CH_2CH_2O)_x\text{-}CH_2C(O)\text{-}O\text{-},$$
$$\text{-}NR_7CH_2CH_2\text{-}O\text{-}(CH_2CH_2O)_x\text{-}CH_2CH_2NR_7\text{-},$$
$$\text{-}SHCH_2CH_2\text{-}O\text{-}(CH_2CH_2O)_x\text{-}CH_2CH_2SH\text{-},$$

wherein

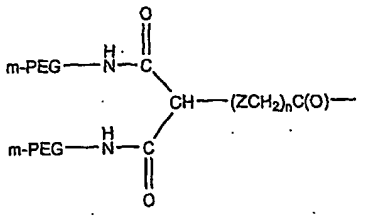
A is a capping group;

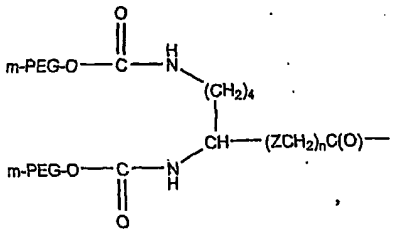
R_7 is selected from hydrogen, $C_{1\text{-}6}$ alkyls, $C_{3\text{-}12}$ branched alkyls, $C_{3\text{-}8}$ cycloalkyls, $C_{1\text{-}6}$ substituted alkyls, $C_{3\text{-}8}$ substituted cycloalkyls, aryls, substituted aryls, aralkyls, $C_{1\text{-}6}$ alkenyls, $C_{3\text{-}12}$ branched alkenyls, $C_{1\text{-}6}$ alkynyls, $C_{3\text{-}12}$ branched alkynyls, $C_{1\text{-}6}$ heteroalkyls, substituted $C_{1\text{-}6}$ hetero-alkyls, $C_{1\text{-}6}$ alkoxyalkyl, phenoxyalkyl and $C_{1\text{-}6}$ heteroalkoxys, and

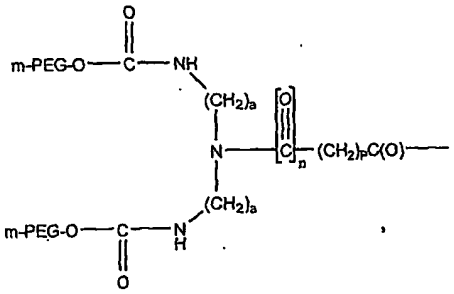
x is the degree of polymerization.

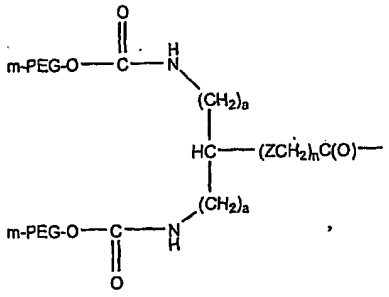
18. The composition of claim 5 where in said capping group is selected from the group consisting of OH, CO_2H, NH_2, SH, and C_{1-6} alkyl moieties.

19. The composition of claim 1 wherein the branched polyalkylene oxide polymer is selected from the group consisting of:









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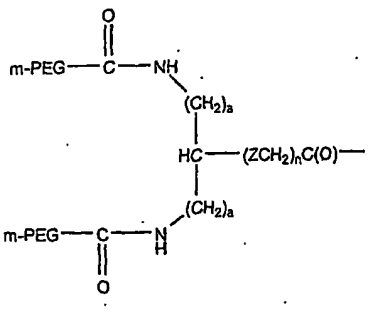


wherein:

(a) is an integer of from about 1 to about 5;

Z is O, NR_8, S, SO or SO_2, where R_8 is H, C_{1-8} alkyl, C_{1-8} branched alkyl, C_{1-8} substituted alkyl, aryl or aralkyl;

(x) is the degree of polymerization;

(n) is 0 or 1;

(p) is a positive integer, preferably from about 1 to about 6;

m-PEG is CH3-O-(CH2CH2O)$_x$-, and

The ligand is interferon-*beta* 1b.

20. The composition of claim 1 wherein the interferon-*beta* 1b comprises the amino acid sequence of SEQ ID NO:1.

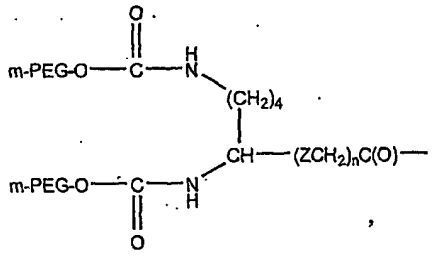
21. The composition of claim 20 wherein the interferon –*beta* 1b is conjugated to a polyalkylene oxide polymer selected from the group selected from:

A- O-$(CH_2CH_2O)_x$-

A-O-$(CH_2CH_2O)_x$-$CH_2C(O)$-O-,

A-O-$(CH_2CH_2O)_x$-CH_2CH_2 NR_7-,

A-O-$(CH_2CH_2O)_x$-CH_2CH_2 SH,



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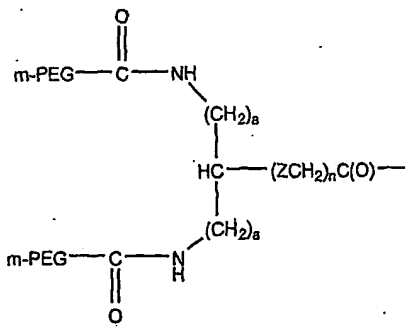


22. The composition of claim 21 wherein the molecular weight of the polyalkylene oxide polymer ranges from about 12kDa to about 60 kDa.

23. The composition of claim 21 wherein the molecular weight of the polyalkylene oxide polymer is about 30 kDa.

24. The composition of claim 21 wherein the molecular weight of the polyalkylene oxide polymer is about 40 kDa.

25. The composition of claim 1 wherein the polyalkylene oxide polymer is conjugated to the interferon-*beta* 1b by a linkage selected from the group consisting of urethane, secondary amine, amide, or thioether.

26. The composition of claim 1 wherein the interferon-*beta* 1b is conjugated to a polyalkylene oxide polymer via the alpha-amino-terminal of the interferon-*beta* 1b.

27. The composition of claim 1 wherein the interferon-*beta* 1b is conjugated to a polyalkylene oxide polymer via an epsilon amino group of a Lys of the interferon-*beta* 1b.

28. The composition of claim 1 wherein the interferon conjugate is present at a concentration of from about 0.01 mg/ml to about 4 mg/ml.

29. The composition of claim 28 wherein the interferon conjugate is present at a concentration of from about 0.05 mg/ml to about 3 mg/ml.

30. A composition comprising:

a) 0.05 to 3.0 mg/ml of interferon *beta* 1b conjugated to a polyalkylene oxide polymer having a molecular weight of at least about 12 kDa,

b) 1% - 5% mannitol, and

c) 3- 10 mM acetic acid

wherein the pH is about 3.7.

31. A biologically-active polymer-interferon conjugate composition of claim 1, wherein at least about 65 percent of the antiviral activity is retained relative to native interferon-*beta* 1b, using the EMC/Vero or EMC/A549 antiviral bioassay.

32. A biologically-active polymer-interferon conjugate composition of claim 1, wherein at least about 20 percent of the antiviral activity is retained relative to native interferon-*beta* 1b, using the EMC/Vero or EMC/A549 antiviral bioassay.

33. A method of preparing the biologically active polymer-interferon conjugate composition of claim 1, comprising reacting interferon-*beta* 1b with an activated polyalkylene oxide polymer having a molecular weight of at least about 30 kDa under conditions sufficient to cause conjugation of the activated polyalkylene oxide polymer to the interferon-*beta* 1b, purifying the resulting conjugate and resuspending the conjugate in a buffered solution having a pH range of about 3.0 to about 8.0, wherein said solution optionally contains an excipient and a surfactant and wherein said composition retains at least about 20% of the antiviral activity is retained relative to native interferon-*beta* 1b, using the EMC/Vero or EMC/A549 antiviral bioassay.

34. The method of claim 33 wherein the conditions are sufficient to cause conjugation of the activated polyalkylene oxide polymer to the amino-terminal of the interferon-*beta* 1b.

35. The method of claim 33 wherein the conditions are sufficient to cause conjugation of the activated polyalkylene oxide polymer to an epsilon amino group of a Lys of the interferon-*beta* 1b.

36. The method of claim 33 wherein the molecular weight of the activated polyalkylene oxide polymer ranges from about 30kDa to about 40 kDa.

37. The method of claim 33 wherein the molecular weight of the activated polyalkylene oxide polymer is about 30 kDa.

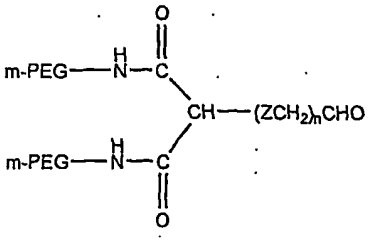
38. The method of claim 33 wherein the molecular weight of the activated polyalkylene polymer is about 40 kDa.

39. The method of claim 33 wherein the activated polyalkylene polymer is an activated polyethylene glycol.

40. The method of claim 39 wherein the activated polyethylene glycol comprises a terminal reactive aldehyde moiety.

41. The method of claim 40 wherein the activated polyethylene glycol is selected from the group consisting of mPEG-$CH_2CH_2CH_2CHO$, mPEG$_2$$CH_2CH_2CH_2CHO$, mPEG-$CH_2CH_2CH_2CH_2CHO$ and mPEG$_2$-$CH_2CH_2CH_2CH_2CHO$.

42. The method of claim 39 wherein the activated polyethylene glycol is selected from the group consisting of



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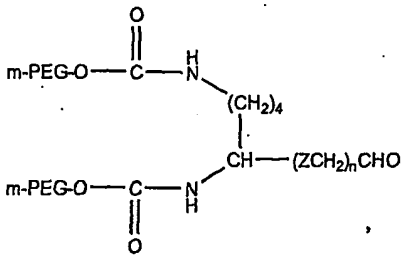

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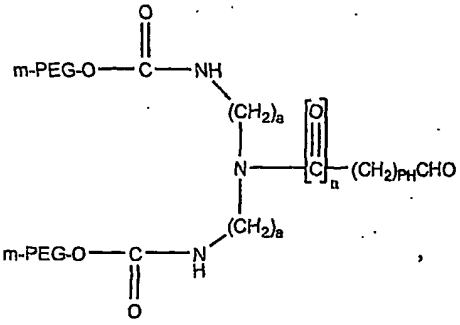

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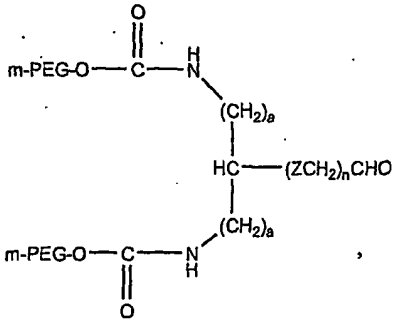

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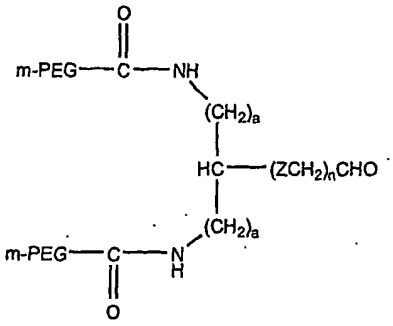

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wherein:

(a) is an integer of from about 1 to about 5;

Z is O, NR_8, S, SO or SO_2, where R_8 is H, C_{1-8} alkyl, C_{1-8} branched alkyl, C_{1-8} substituted alkyl, aryl or aralkyl;

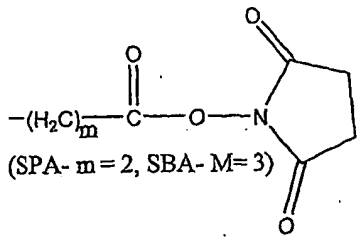
(x) is the degree of polymerization;

(n) is 0 or 1;

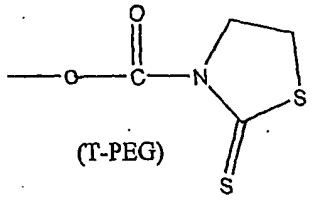
(p) is a positive integer, preferably from about 1 to about 6, and

m-PEG is $CH3-O-(CH2CH2O)_x-$.

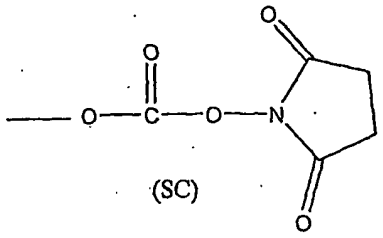
43. The method of claim 33, wherein the activated polyethylene glycol comprises a terminal reactive moiety selected from the group consisting of:



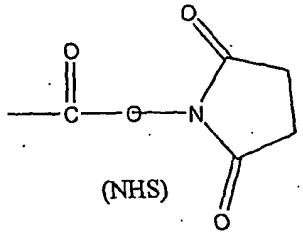
(SPA- m = 2, SBA- M= 3)



(T-PEG)



(SC)



(NHS)

44. A method of administering a composition of claim 1 comprising a first step of neutralizing the acidic buffers followed by administering the composition to a patient in need of such administration.

45 The method of claim 44 wherein the acidic buffer is neutralized with sodium phosphate.

46. The method of claim 44 wherein the composition is administered orally, intravenously, subcutaneously, or intramuscularly.

47. A method of treating a mammal having a disease or disorder responsive to interferon-*beta* comprising administering an amount of the pharmaceutical composition of claim 1 effective to treat the disease or disorder.

48. A method of preparing a polyalkylene oxide-protein conjugate comprising the steps of

(a) solubilizing a protein of interest in a compatible aqueous solution in the presence of a protein-solubilizing amount of a compatible detergent;

(b) reacting the solubilized protein of interest with an activated polyalkylene oxide polymer, to produce a solution comprising a polyalkylene oxide-protein conjugate and the detergent;

(c) adjusting the reacted solution of step (b) to a pH effective to dissociate the detergent from the polyalkylene oxide-protein conjugate;

(d) separating the dissociated detergent from the polyalkylene oxide-protein conjugate, and recovering the polyalkylene oxide-protein conjugate.

49. The method of claim 48 wherein pH is adjusted in step (c) to a range from about pH 3 to about pH 4.

50. The method of claim 48 wherein the activated polyalkylene oxide polymer is a polyethyelene glycol polymer ranging in size from about 12kDa to about 60 kDa.

51. The method of claim 48 wherein the detergent is selected from the group consisting of an ionic detergent, a non-ionic detergent, a zwitterionic detergent, and combinations thereof.

52. The method of claim 51 wherein the detergent is a zwitterionic detergent.

53. The method of claim 48 wherein the protein is an interferon.

54. The method of claim 53 wherein the protein is an IFN-*beta*.